REMARKS

Claims 1-5, 7-28, 30 and 31 are pending in the application. Claims 6 and 29 were previously cancelled. Claim 3 is cancelled herein. Thus, claims 1, 2, 4, 5, 7-28, 30 and 31 are under consideration. Claims 1, 2, 5, 7, 9-12, 16 and 31 are amended herein. No new matter is added by these amendments. Support for these amendments is found throughout the as-filed specification and original claims. Each of the Examiner's specific rejections are addressed below.

I. Interview summary.

The Applicants thank Examiner Olsen for the in-person interview on June 03, 2011, in which the 35 U.S.C. § 112 and 35 U.S.C. § 103(a) rejections were discussed without reaching agreement.

II. 35 U.S.C. § 112, first paragraph.

Claims 2 and 3 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Claim 3 is cancelled herein rendering the rejection moot as to claim 3. In regard to claim 2, while the Applicants believe the original claim is enabled, Applicants herein amend claim 2 to expedite its allowance. Specifically, claim 2 has been amended to delete cell types other than erythrocytes and leukocytes. Since the Examiner indicates that claim 2 is enabled for erythrocytes and leukocytes, Applicants respectfully request withdrawal of this rejection. Moreover, the Applicants specifically reserve the right to pursue the deleted cell types in a divisional or continuation application.

Claim 31 is rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Claim 31 is amended herein for greater clarity. The Applicants respectfully request that the Examiner reconsider this rejection in light of the amendment and comments provided below.

Amended claim 31 recites that movement of the desired cell type through the membrane due to electric potential is substantially greater than any convective movement of the desired cell through the membrane. The Examiner acknowledges that the application teaches that the ion-permeable barriers (e.g. membranes) substantially prevent convective movement. The Examiner also acknowledges that the application teaches that a cell type is separated through the membrane. The application, therefore, also teaches significantly greater movement of the desired cell type thought the membrane by electric potential versus convective movement. For example, page 3, lines 29-30, indicate that substantially all trans-barrier migration of the desired cell type(s) occurs upon the application of the electric potential. For at least these reasons, claim 31 as amended is supported by the as-filed application. The Applicants respectfully request withdrawal of this rejection.

III. 35 U.S.C. § 103 (a)

Claims 1-28, 30 and 31 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,491,819 (Prince) in view of CN 1048168A (Su) or U.S. Patent No. 7,214,299 (Armstrong) and U.S. Patent Publication No. 2002/0043465 (Vigh).

Claim 6 was previously cancelled and claim 3 is cancelled herein. The rejection is therefore moot regarding these claims.

Claim 1 has been amended to recite ion-permeable membrane rather than ion-permeable barrier. As discussed above, support for ion-permeable membrane is found throughout the as-filed application including the original claims. For example, support for this amendment is found at paragraphs 0052 and 0053.

The combined references fail to establish a *prima facia* case of obviousness of claim 1 or the remainder of the rejected claims, which all ultimately depend from claim 1. The combined references fail to establish *prima facia* obviousness of the rejected claims because (a) the combined references fail to teach or suggest all the limitations of the rejected claims, (b) there is no suggestion or motivation to modify the references to arrive at the processes of the rejected claims, and a device based on the combined references would not function as intended or provide

a predictable solution or results, and (c) there would be no reasonable expectation of success to combine the references to arrive at the process of the rejected claims.

(a) The combined references fail to teach or suggest all the limitations of the rejected claims.

The combination of Prince in view of Su or Armstrong and in further view of Vigh do not disclose or suggest all the limitations of claim 1. To establish a *prima facia* case of obviousness, all of the claim limitations must be taught or suggested by the prior art. *In re Royka* 490 F.2d 981 (CCPA 1974). The combined references do not, however, teach or suggest all of the limitations of all the rejected claims.

For example, the combined references do not teach or suggest applying an electric potential to cause at least one cell type to move through an ion-permeable membrane for separation of a cell type from a mixture of cell types by electrophoresis. The cited references also fail to teach or suggest causing at least one cell type to move through an ion-permeable membrane, wherein substantially all of the transmembrane migration of a desired cell type occurs upon the application of the electric potential.

As recognized by the Examiner, Prince does not disclose separation of cells through a membrane using electrophoresis. The Examiner cites Su, or alternatively, Armstrong for showing separation of cells through an ion-permeable barrier using electrophoresis. The Examiner also alleges that Su and Armstrong each teach substantially all transmembrane movement of a desired cell type upon the application of electric potential. Neither Su or Armstrong, however, teach the use of electric potential to move cells through a membrane or teach substantially all transmembrane movement using electric potential.

In regard to Su, the reference fails to disclose separation of a cell type by moving a cell through an ion-permeable membrane where the cell type is separated through the ion-permeable membrane upon application of an electric field. Therefore, by necessity, Su also fails to show substantially all movement of a desired cell type upon the application of electric potential.

The figures from Su, viewed with reference to pages 4-6 of the Su description, show that the electrodes (2 and 5) are located outside of an electrophoresis cell (4). The electrophoresis cell is the semi-permeable bag (e.g. membrane) and the electrodes are outside of the semi-permeable bag.

Therefore, when a sperm sample is placed inside the cell it is separated from the electrodes, including the anode, by the bag's walls. Su does not teach movement of sperm through the bag's walls and, moreover, Su actually teaches away from moving sperm though an ion-permeable membrane.

Su teaches that semen is collected "at the anode." The term "at" does not, however, necessarily mean or imply direct contact of semen with the anode. Common definitions of the term "at" include "in or near the area occupied by" or "in or near the location of." See definition 1.a. of "At" from the Free Online Dictionary, Thesaurus and Encyclopedia (Exhibit A). The semen found "at the anode" could, therefore, be near or in the area of the anode without having passed through the bag's walls. For example, the semen could be contained in the electrophoresis cell in proximity to the anode, but still separated from the anode by the chamber walls.

Just because Su collected an enhanced population of X semen at the anode, it does not mean that the collected X semen must have moved through a membrane. In fact, Su describes that the semi-permeable bag is actually used to *prevent* direct contact between semen and the [anode]. For example, on page 5 Su states "the design of the electrophoresis cell used can prevent direct contact between the semen and the electrodes."

Thus, based on the common definition of "at" and the explicit teaching of Su, the semen does not appear to contact the anode at all and, therefore, Su intentionally avoids passing sperm through an ion-permeable membrane to avoid contact of semen with the electrodes.

For at least these reasons, Su does not show separation of a cell type by movement of a cell through an ion-permeable membrane. And, therefore, the combination of Prince and Su does not teach or suggest movement of a cell through a membrane upon application of an electric potential.

Even if the Examiner were to maintain that the movement of cells with Su could be combined with the membrane of Prince, this combination still fails to teach or suggest substantially all transmembrane migration of a desired cell type upon application of electric potential, which is a separate element of claim 1. Thus, for both of these reasons, the combination of Prince and Su does not teach or suggest all limitations of the rejected claims. Since Vigh does nothing to remedy these defects, the cited combination of Prince, Su and Vigh do not disclose or suggest the process of claim 1-28, 30 and 31, and the Applicants request that the rejection based on these references be withdrawn.

In regard to Prince in view of Armstrong and in further view of Vigh, the Armstrong reference teaches that separation is accomplished through a soluble polymer. For example, in column 7, lines 38-40, Armstrong states that the polymer must be soluble and/or dispersible in aqueous solution. Therefore, the combination of Armstrong and Prince fails to show separation of a cell type by movement through an ion-permeable membrane upon application of electric potential. Moreover, Prince and Armstrong fail to teach or suggest substantially all transmembrane migration of a desired cell type upon application of electric potential. Since Vigh does nothing to remedy this defect, the cited combination of Prince, Armstrong and Vigh do not disclose or suggest the process of the rejected claims, and the Applicants request that the rejection of claim 1-28, 30 and 31 based on these references be withdrawn.

(b) There is no suggestion or motivation to modify the references to arrive at the process of the rejected claims, and a device based on the combined references would not function as intended or provide a predictable solution or results.

Prince passes cells through a membrane by transmembrane pressure created by fluid flow. Prince does not teach or suggest use of electric potential to accomplish transmembrane migration. In addition, neither Su nor Armstrong teach or suggest movement of cells through a membrane using electric potential. In fact, Su teaches away from movement of cells through a membrane using electric potential by stating that the membrane prevents such movement. Armstrong also teaches away from movement of cells through a membrane using electric

potential by stating movement must be in a soluble polymer. Thus, one skilled in the art would not be motivated to modify Prince based on Su or Armstrong to use electric potential because both teach or suggest impeded movement of cells though a membrane.

In addition, one skilled in the art would not expect predictable results from a device based on the cited combination of references. For example, referring to Figure 8 of Prince, for an electrical potential to function analogously to the transverse pressure flow in Prince it would need to be applied perpendicular to the membrane surface 40. To effectuate such an electric potential, electrodes would need to be positioned on either side of the membrane 40. *E.g.* one electrode would need to be located interior to the membrane and one exterior to the membrane. As described in Prince, cells flow through the membrane 40 and into the central manifold 48. *See e.g.* Prince column 13, lines 39-46. The cells in the central manifold then move out of the outlet 30 for collection in the filtrate collection bag 62. See *Id.*

If Prince were modified to include electrodes, then the electrode interior to the membrane would attract cells that flowed through the membrane. One skilled in the art would, therefore, expect this electrode to impede cell flow to the filtrate collection bag 62 since the cells would collect internally at the electrode by the same attractive force creating the transverse movement. Similarly, one skilled in the art would expect cells to be attracted to an outer electrode causing an impediment to accumulation cells at the cell reservoir 55. Furthermore, the magnetic drive, described in column 12, lines 27-42, would distort any applied electrical field rending a non-uniform application of an electrical field through the membrane.

Thus, one skilled in the art would not predict that a device combining Prince and Su or Armstrong would function as intended in Prince if electrical potential was used to replace the flow-based transmembrane pressure. At the least, the combining step would require additional effort such that it would not have been taken by one skilled in the art without a recognized reason to do so. No such reason has been offered by the Examiner. Therefore, one skilled in the art would not modify Prince by the combination of these references as suggested by the Examiner and would not predict the combined elements to provide predictable results. The *prima facia*

case of obviousness is therefore improper and the Applicants request that the rejection of claim 1-28, 30 and 31 based on these references be withdrawn.

(c) There would be no reasonable expectation of success for the cited combination of references.

As described under the previous heading and again referring to Figure 8 of Prince, for an electrical potential to function analogously to the transverse pressure flow in Prince it would need to be applied perpendicular to the membrane surface 40. To effectuate such an electric potential, electrodes would need to be positioned on either side of the membrane 40. *E.g.* one electrode would need to be located interior to the membrane and one exterior to the membrane. As described in Prince, cells flow through the membrane 40 and into the central manifold 48. *See e.g.* Prince column 13, lines 39-46. The cells in the central manifold then move out of the outlet 30 for collection in the filtrate collection bag 62. See *Id.*

If Prince were modified to include electrodes, then the electrode interior to the membrane would attract cells that flowed through the membrane. One skilled in the art would, therefore, expect this electrode to impede cell flow to the filtrate collection bag 62 since the cells would collect internally at the electrode by the same attractive force that would be creating the transverse movement. Similarly, one skilled in the art to expect cells would be attracted to the outer electrode causing an impediment to accumulation of cells at the cell reservoir 55. Furthermore, the magnetic drive, described in column 12, lines 27-42, would distort any applied electrical field rending a non-uniform application of an electrical field through the membrane.

Thus, a device combining Prince and Su or Armstrong would not reasonably be expected to function as described in Prince if electrical potential was used to replace the flow-based transmembrane pressure. In fact, one skilled in the art would expect that such a combination, and the resulting modification of Prince, would render Prince unsatisfactory for its intended purpose. For this reason, the *prima facia* case of obviousness is improper for the rejected claims and the Applicants request that the rejection of claim 1-28, 30 and 31 based on these references be withdrawn

IV. Conclusions

It is believed that all issues raised by the Examiner have been addressed. However, the absence of a reply to a specific rejection, issue, or comment does not signify agreement with or concession of that rejection, issue, or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

Applicants wish to call the Examiner's attention to co-pending U.S. Patent Publication No. 2009/0101507 and encourage the Examiner to review this application and its corresponding file history.

Fees in the amount of $555.00 for a 3-month extension of time for a small entity are being paid concurrently herewith on the Electronic Filing System by way of Electronic Funds Transfer authorization. Please apply any other charges or credits to Deposit Account 50-5226.

Respectfully submitted,

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